VANCOMYCIN RESISTANT (INTERMEDIATE) STAPHYLOCOCCUS AUREUS
(VRSA/VISA)

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

Staphylococcus aureus (Staph aureus) can cause a variety of skin and soft tissue infections, as well as cause invasive disease including bacteremia, endocarditis, toxic shock syndrome, etc., Staphylococci produce a variety of extracellular pathogenic factors that are responsible for many of the disease manifestations including toxins (poisons), leukocidins (ability to destroy white blood cells) and hemolysins (the ability to destroy red blood cells) as well as the ability to produce biofilms and capsules (which help bacteria evade the immune system).

Causative Agent:

Staph aureus is a gram positive cocci (bacteria). VRSA (VISA) are bacteria that have acquired resistance (complete or intermediate resistance) to a glycopeptide antibiotic known as vancomycin.

NOTE: VRSA/VISA is NOT MRSA (methicillin resistant *Staphylococcus aureus*). There have only been 6 cases of VRSA and 16 cases of VISA reported in the U.S.

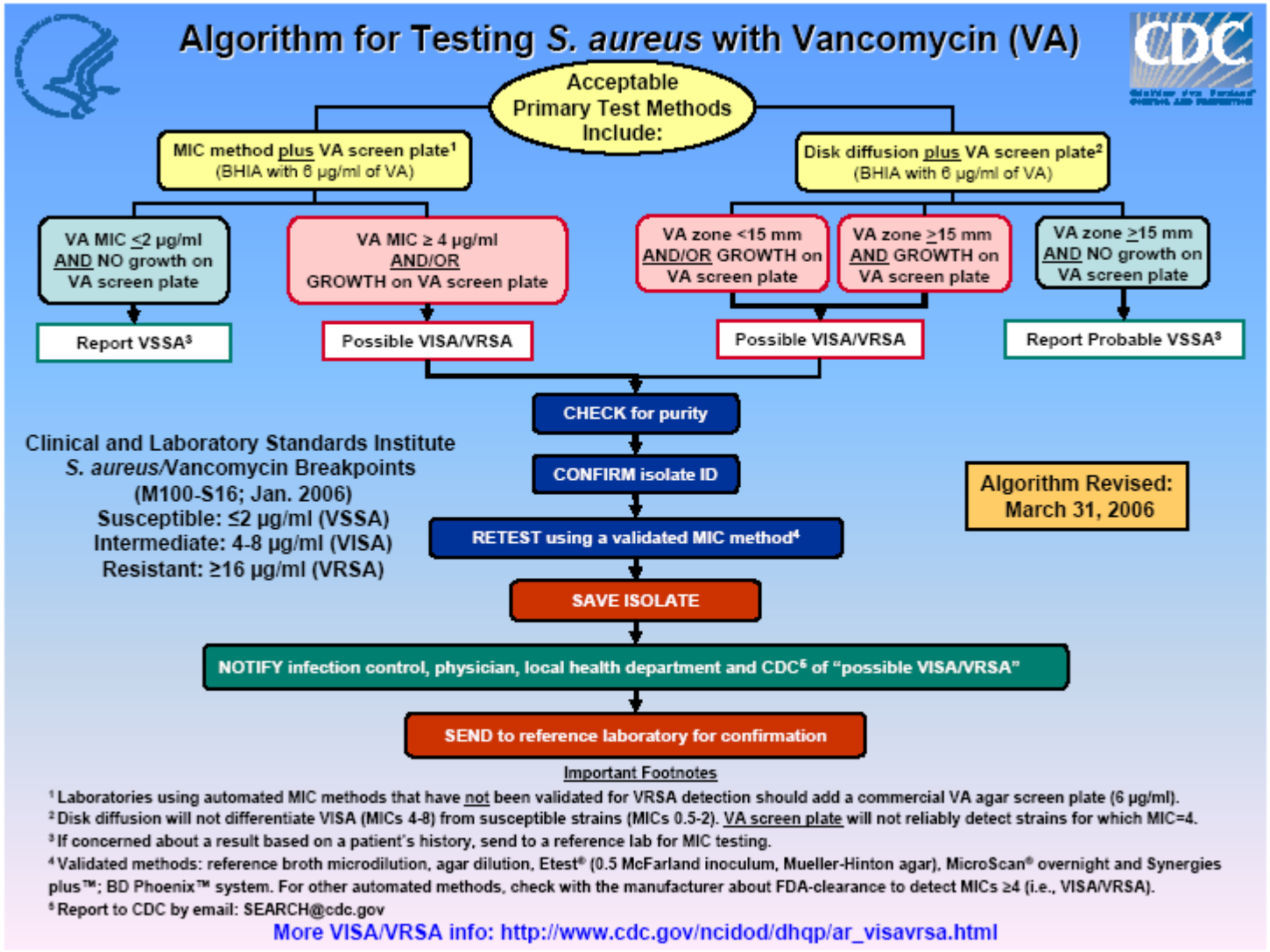
Differential Diagnosis:

Vancomycin and teicoplanin are glycopeptides antibiotics. If a Staph aureus is resistant to both of these antibiotics, it would be known as glycopeptides resistant/intermediate Staph aureus or GRSA/GISA.

Laboratory identification:

The following algorithm demonstrates the appropriate laboratory identification schema. Additional information can be found at:
http://www.cdc.gov/ncidod/dhqp/ar_visavrsa_lab.html

It is important to recognize that automated testing methods commonly located in laboratories may not reliably detect this organism.


Algorithm for Testing S. aureus with Vancomycin (VA)
CDC
Acceptable Primary Test Methods Include:
MIC method plus VA screen plate[1] (BHIA with 6 µg/ml of VA)
Disk diffusion plus VA screen plate[2] (BHIA with 6 µg/ml of VA)
VA MIC ≤2 µg/ml AND NO growth on VA screen plate
VA MIC ≥ 4 µg/ml AND/OR GROWTH on VA screen plate
VA zone <15 mm AND/OR GROWTH on VA screen plate
VA zone ≥15 mm AND GROWTH on VA screen plate
VA zone ≥15 mm AND NO growth on VA screen plate
Report VSSA[3]
Possible VISA/VRSA
Possible VISA/VRSA
Report Probable VSSA[3]
CHECK for purity
CONFIRM isolate ID
RETEST using a validated MIC method[4]
SAVE ISOLATE
NOTIFY infection control, physician, local health department and CDC[5] of "possible VISA/VRSA"
SEND to reference laboratory for confirmation
Clinical and Laboratory Standards Institute
S. aureus/Vancomycin Breakpoints
(M100-S16; Jan. 2006)
Susceptible: ≤2 µg/ml (VSSA)
Intermediate: 4-8 µg/ml (VISA)
Resistant: ≥16 µg/ml (VRSA)
Algorithm Revised: March 31, 2006
Important Footnotes
[1] Laboratories using automated MIC methods that have not been validated for VRSA detection should add a commercial VA agar screen plate (6 µg/ml).
[2] Disk diffusion will not differentiate VISA (MICs 4-8) from susceptible strains (MICs 0.5-2). VA screen plate will not reliably detect strains for which MIC=4.
[3] If concerned about a result based on a patient's history, send to a reference lab for MIC testing.
[4] Validated methods: reference broth microdilution, agar dilution, Etest® (0.5 McFarland inoculum, Mueller-Hinton agar), MicroScan® overnight and Synergies plus™; BD Phoenix™ system. For other automated methods, check with the manufacturer about FDA-clearance to detect MICs ≥4 (i.e., VISA/VRSA).
[5] Report to CDC by email: SEARCH@cdc.gov
More VISA/VRSA info: http://www.cdc.gov/ncidod/dhqp/ar_visavrsa.html

Treatment:
To date, all cases of VISA and VRSA have been susceptible to other licensed antibiotics. There is concern however, about the possibility that an extremely-resistant bacteria could emerge from a case of VISA/VRSA, thus the cause for concern.

The decision to decolonize carriers should be made by the primary care physician in conjunction with hospital infection control and public health.

Case fatality:
If the organism is susceptible to licensed antibiotics, the case fatality should approximate that of non VRSA/VISA organisms. If the organism is resistant to licensed antibiotics, then the case fatality rate could rise.

Reservoir:
Staph aureus is found in mammals and birds and routinely colonizes skin and mucosal surfaces.

Transmission:
Staph aureus is transmitted from person to person by direct contact.

Susceptibility:
While all people are susceptible to Staph infections, individuals who have had long term antimicrobial therapy for multiply resistant organisms (especially vancomycin resistant enterococci) are at highest risk of developing this infection.

Incubation period:
Not applicable.

Period of communicability:
This is communicable until the patient has completed appropriate therapy.

Epidemiology:
At the time of this document, there have been 6 cases of VRSA and 16 cases of VISA identified in the United States. It is important to reinforce with hospitals, clinicians, and laboratories that identification of this organism is an important event with critical infection control elements that must be instituted. This infection, at this time, results from long term therapy with antibiotics (especially vancomycin).

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:
- **IMMEDIATELY NOTIFY UDOH AND HOSPITAL INFECTION CONTROL. VISA or VRSA are infection control emergencies.**
- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.

- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.

Prevention:

The likelihood of acquiring this disease are minimized by judicious use of antibiotics when treating individuals with severe infections, along with appropriate handwashing and other infection control measures.

Chemoprophylaxis:

The decision to decolonize healthcare workers should be made by occupational health services, the infection control team, the healthcare worker, public health, and the worker's personal physician.

The decision to decolonize non-healthcare worker contacts should be made by the contact, their primary care physician, and public health authorities.

Vaccine:

None.

Isolation and quarantine requirements:

Isolation: Cases will be strictly isolated. See case investigation process.
Hospital: Hospitals will institute strict infection control policies. See case investigation process. These are listed at: http://www.cdc.gov/ncidod/dhqp/ar_visavrsa_prevention.html
Quarantine: Quarantine measures on colonized individuals are possible. See case investigation process.

✓CASE INVESTIGATION

Reporting:

Reporting refers to the process of healthcare providers or institutions (e.g., clinicians, clinical laboratories, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. Cases of illness may also be ascertained by the secondary analysis of administrative health data or clinical data. The purpose of this section is to provide those criteria that should be used by humans and machines to determine whether a specific illness should be reported.

VISA: Report any isolation of *S. aureus* from any body site that has a minimum inhibitory concentration 4–8 μg/ml, as detected and defined according to Clinical and Laboratory Standards Institute approved standards and recommendations (CLSI 2006).

VRSA: Report any isolation of *S. aureus* from any body site that has a minimum inhibitory concentration ≥ 16 μg/ml, as detected and defined according to Clinical and Laboratory Standards Institute approved standards and recommendations (CLSI 2006).

Report any person whose healthcare record contains a diagnosis of *Staphylococcus aureus* infection/colonization intermediate or resistant to vancomycin.

Report any person whose death certificate lists *Staphylococcus aureus* infection intermediate or resistant to vancomycin as a cause of death or a significant condition contributing to death.

Other recommended reporting procedures

- All cases of *Staphylococcus aureus* infection/colonization with intermediate or resistant to vancomycin should be reported.
- Reporting should be on-going and routine.
- Frequency of reporting should follow the state health department's routine schedule.

Table of criteria to determine whether a VISA/VRSA case should be reported to public health authorities

Criterion	Reporting		Confirmed VISA	Confirmed VRSA
Clinical Presentation				
healthcare record contains a diagnosis of *Staphylococcus aureus* infection intermediate or resistant to vancomycin		S		
Death certificate lists *Staphylococcus aureus* infection intermediate or resistant to vancomycin as a cause of death or a significant condition contributing to death		S		
Laboratory Findings				
Isolation of *S. aureus* from any body site			N	N
Resistance of the S. aureus isolate to vancomycin (Minimum Inhibitory Concentration [MIC] ≥16 μg/ml)†				N
Intermediate resistance of the S. aureus isolate to vancomycin (Minimum Inhibitory Concentration [MIC] 4–8 μg/ml)†			N	

Notes:
S = This criterion alone is sufficient to report a case.
N = This criterion in conjunction with all other "N" criteria in the same column is required to report a case.
†detected and defined according to Clinical and Laboratory Standards Institute approved standards and recommendations (CLSI 2006).

Case definition:
VRSA/VISA (CDC 2010):

Clinical Description

S. aureus can produce a variety of syndromes with clinical manifestations including skin and soft tissue infections, empyema, bloodstream infection, pneumonia, osteomyelitis, septic arthritis, endocarditis, sepsis, and meningitis. S. aureus may also colonize individuals who remain asymptomatic. The most frequent site of S. aureus colonization is the nares.

Laboratory Criteria

VISA:

- Isolation of *S. aureus* from any body site.
  AND

- Intermediate susceptibility of the *S. aureus* isolate to vancomycin, detected and defined according to Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) approved standards and recommendations (Minimum Inhibitory Concentration [MIC] = 4-8 μg/ml).

VRSA:

- Isolation of *S. aureus* from any body site.
  AND
- *S. aureus* isolate resistant to vancomycin, detected and defined according to Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) approved standards and recommendations (Minimum Inhibitory Concentration [MIC] ≥ 16 μg/ml).

Case Classification

VISA:

Confirmed: A case of *S, aureus* that has intermediate susceptibility to vancomycin that is laboratory-confirmed (MIC = 4-8 μg/ml).

VRSA:

Confirmed: A case of vancomycin-resistant *S. aureus* that is laboratory-confirmed (MIC ≥ 16 μg/ml for VRSA).

Classification Table

Criteria for defining a case of VISA/VRSA

Criterion	Confirmed VISA	Confirmed VRSA
Clinical Presentation		
healthcare record contains a diagnosis of *Staphylococcus aureus* infection intermediate or resistant to vancomycin		
Death certificate lists *Staphylococcus aureus* infection intermediate or resistant to vancomycin as a cause of death or a significant condition contributing to death		
Laboratory Findings		
Isolation of *S. aureus* from any body site	N	N
Resistance of the S. aureus isolate to vancomycin (Minimum Inhibitory Concentration [MIC] ≥16 μg/ml) †		N
Intermediate resistance of the S. aureus isolate to vancomycin (Minimum Inhibitory Concentration [MIC] 4-8 μg/ml) †	N	

Case Investigation Process:

- **Immediately notify UDOH and the ICP at the local hospital.**

- All further steps of the case investigation will be carried out with representatives from the CDC, UDOH, LHD, and hospital.
  - Develop a written plan to determine infection control actions that will be taken with all individuals who are identified as carriers. This plan must include treatment protocols, follow-up cultures (how and when obtained), when carriers will be considered free of colonization, and quarantine protocols for carriers. This plan should be written and agreed upon prior to any culture workups of contacts.
  - All contacts should be identified and categorized as extensive, moderate, or minimal, according to their level of interaction with the colonized or infected patient.
    - As a first step, identify all contacts with extensive interaction with the patient based upon a defined period before the first culture date. Examples of extensive interaction would involve:
      - Patients who shared a room with the case patient.
      - Healthcare providers and staff who:
        - Clean/bathe/rotate/ambulate the patient
        - Change dressings
        - Make more than 3 visits per day to the patient
        - Handle secretions and body fluids (including respiratory secretions)
        - Care for wound dressings or perform debridement
        - Conduct physical exams on the patient
        - Have documented prolonged patient contact, including physical therapy, rehabilitation personnel, dialysis, and respiratory technicians
      - Family members who:
        - Provide primary care
        - Have close contact with patient (e.g., sleep in the same bed, or same room)
    - Examples of moderate interaction include:
      - Healthcare providers and staff who:
        - Deliver medications
        - Cross-cover patient only
        - See the patient on daily rounds, without conducting extensive exams
        - Perform surgical or invasive procedures where sterile barriers or aseptic techniques are used.
        - Monitory patient-care equipment without handling secretions
        - Have limited interactions (e.g. radiology technicians)
    - Examples of minimal interaction include:
      - Healthcare providers and staff who:
        - Work on the same floor without formal cross-coverage of patient
        - Perform predominately administrative duties
        - Consult without extensive exam
        - Visit during teaching rounds only
        - Provide dietary or maintenance services that do not interact directly with the patient
  - Collect surveillance cultures
    - Patient:
      - Culture nares, wounds, drains, and other clinically relevant sites.
      - Consider determining whether patient also carries VRE.
    - Healthcare providers and staff with extensive interaction:
      - Culture nares and all skin lesions/wounds.

    - If no one in this group is identified as colonized with VRSA/VISA, then do not continue with surveillance cultures for individuals with moderate or minimal interaction.
- If VISA/VRSA colonization of contacts is identified OR until the case is no longer colonized or infected:
    - Culture the nares of contacts with extensive interaction (weekly) to assess the efficacy of infection control precautions.
    - Place a log book at the entrance of the patient's room to identify and track patient contacts.

Outbreaks:

An outbreak will be defined as: a single case of VRSA/VISA in Utah.

Identification of case contacts:

See above.

Case contact management:

See above.

✓REFERENCES

Principles and Practice of Infectious Disease (6th Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

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Hageman JC, Patel JB, Carey RC, Tenover FC, and Mcdonald LC. Investigation and Control of Vancomycin-Intermediate and –Resistant *Staphylococcus aureus*: A Guide for Health Departments and Infection Control Personnel, Atlanta GA, 2006.

Clinical and Laboratory Standards Institute/NCCLS. Performance Standards for Antimicrobial Susceptibility Testing. Sixteenth informational supplement. M100-S16. Wayne, PA: CLSI, 2006.